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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
[illegible]	[illegible]	[illegible]	[illegible]

HM12/1002

[illegible]
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EXAMINER	
[illegible]	
ART UNIT	**PAPER NUMBER**
1636	6

DATE MAILED: 10/02/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev. 2/95)
*U.S. GPO 2000-473-000/44602

1- File Copy

Office Action Summary	Application No. 09/580,476	Applicant(s) WESTAWAY ET AL.
	Examiner David Guzo	Art Unit 1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-65 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-65 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4 .
4) ☐ Interview Summary (PTO-413) Paper No(s) _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other.

DETAILED ACTION

1. Acknowledgment is made of applicant's claim for foreign priority based on applications filed in Australia on 11/28/97 and 9/23/98. It is noted, however, that applicant has not filed a certified copy of the Australian applications as required by 35 U.S.C. 119(b) and has not perfected the claim for foreign priority.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-4, 6-20, 24-32, 35-39, 43-53, 55-64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a gene expression and delivery system comprising a replicon of the Kunjin virus and a second vector capable of expressing Kunjin virus structural proteins, cell lines stably transformed with the Kunjin replicon, methods of producing said cell lines, methods of producing Kunjin particles, and DNA based Kunjin virus replicon vectors, does not reasonably provide enablement for a gene expression and delivery system comprising a replicon derived from any flavivirus and a second vector capable of expressing any flavivirus structural protein, cell lines stably transformed with said replicons,

methods of making any flavivirus particles, any flavivirus DNA based replicon vectors, etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is whether the skilled artisan could make and use the claimed invention from the teachings of the application coupled with information in the art without undue experimentation (*United States v. Telectronics Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based upon a single factor, but instead is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

1) Unpredictability of the art. The art in the area of flavivirus expression vectors is unpredictable. The flavivirus group of viruses is comprised of a large number of poorly characterized viruses, most of which have not been genetically manipulated with regard to generation of recombinant expression systems. While the flaviviruses share some common features with regard to genome organization, they share little sequence homology. The packaging mechanisms for flavivirus RNA were unknown at the time of applicants' invention. Many flaviviral proteins can be cytotoxic to cells and the skilled artisan would need to develop cell lines which could support replication of flavivirus replicons and expression of cytotoxic flavivirus proteins. The cell lines would also need to be capable of supporting expression of flavivirus proteins necessary to complement *in trans* the

deleted flaviviral structural proteins. This would involve essentially trial and error experimentation with no guidance from applicants.

2) State of the art. The state of the art with regard to the generation of recombinant flavivirus expression vectors and replicons is poorly developed.

3) Number of working examples. Applicants present working examples only using the Kunjin virus.

4) Scope of the claims. The claims are broad and read on the generation of gene expression and delivery systems derived from any of the approximately 70 flaviviruses, stably transformed cell lines capable of expressing flavivirus proteins and supporting flavivirus replicons, any flavivirus particles generated from the producer cell lines, etc.

5) Amount of guidance provided by applicants. Applicants provide no guidance on the generation of non-Kunjin derived gene expression and delivery systems, no guidance on the generation of cells stably transformed with flaviviral replicons, no guidance on the generation of non-Kunjin recombinant flaviviral particles, etc.

6) Nature of the invention. The invention involves a complex and poorly understood area of molecular biology; the generation of recombinant flaviviral gene expression and delivery systems.

7) Level of skill in the art. The level of skill in the art is high; however, given the unpredictability of the art, the poorly developed state of the art, the lack of guidance provided by applicants and the broad scope of the invention, it must be considered that the skilled artisan would have had to

have conducted trial and error experimentation in order to attempt to practice the claimed invention.

4. Claims 1-4, 6-20, 24-32, 35-39, 43-53, 55-64 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim a genus of flavivirus replicons, a genus of cells stably transformed with said replicons, flavivirus particles produced from said cells, a genus of DNA based replicon vectors of flavivirus origin, etc. Applicants provide a written description of Kunjin virus replicons, gene expression and delivery systems derived from Kunjin virus, cell lines stably transformed with Kunjin virus replicons, methods of making Kunjin virus particles from the transformed cell lines, vectors capable of expressing Kunjin viral structural proteins, etc.

The written description requirement for a claimed genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics sufficient to show applicants were in possession of the claimed genus. In the instant case,

applicants provide no description of flavivirus gene expression and delivery systems other than those derived from Kunjin virus, no description of cells stably transformed with flavivirus replicons other than those derived from Kunjin virus, no description of making any flavivirus particles other than Kunjin virus particles, no DNA based replicon vectors other than those derived from Kunjin virus, etc. Applicants claim the recited flavivirus vectors, cell lines, etc. by functional characteristics only and present no correlation between structure and function, i.e. applicants present no correlation between the structures of the other flavivirus vectors, replicons, transformed cell lines, etc. and the functions of said vectors, replicons, cell lines, etc. encompassed by the claims. Given the wide diversity of viruses encompassed by the claims, the unpredictability of the art in this area, the poorly developed state of the art and the lack of a written description of the invention other than that derived from Kunjin virus, the skilled artisan would conclude that applicants were not in possession of the claimed genus.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (and dependent claims) is vague in that while applicants recite a "second vector" in part (b) of the claim, the claim does not recite a first vector. Claim 1 is also vague in the recitation of the phrase "...vector is engineered to prevent recombination with the replicon..." because it is unclear what techniques are encompassed within this terminology, i.e. how is the vector engineered to prevent recombination?

Claims 6 and 44 (and dependent claims) is vague in the recitation of a vector "...engineered to prevent recombination..." with the self-replicating vector. Again the metes and bounds of how the vector is manipulated to prevent recombination are unclear. Claim 6 is also vague in the phrase "...does not encode for the structural protein..." as this language is confusing. Redrafting the claim to read as "does not encode the structural protein" would be remedial.

Claims 11 and 60 are vague in the recitation of the phrase "...inserted within the locality of at least a deleted gene..." since the metes and bounds of the term "locality" are unclear, i.e. how far from the deleted gene is "within the locality" of the gene.

Claims 22, 23, 37-40 are vague in the term "as herein described" as this terminology is redundant and adds nothing to the claimed expression systems.

Claim 37 is vague in the phrase "...core protein an the second vector...". Possibly redrafting the claim to read as "core protein and the second vector" would be remedial.

Claims 43 and 44 (and dependent claims) are vague in the recitation of the phrase "...all or part of a structural protein(s) region and or a protein(s)or part thereof required for packaging..." as the

metes and bounds of the claim are unclear. It is unclear if the claim encompasses deleted structural proteins **and** proteins required for packaging the genome in flavivirus particles, etc.

Claim 46 is vague in the recitation of the phrase "contains replicon that". Insertion of "a" between "contains" and "replicon" would be remedial.

In Claim 48, line 6, the ";" between "promoter" and "5'" should be deleted as it makes no sense in this location.

In Claim 49, line 2, the term "6' untranslated region" should be "5' untranslated region".

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Robert Schwartzman, can be reached on (703) 308-7307. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding or relating to attachments to this Office Action should be directed to Patent Analyst Zeta Adams whose telephone number is (703) 305-3291.

David Guzo
October 1, 2001

DAVID GUZO
PRIMARY EXAMINER